A

```
-51  MEQRGQMAPAASGARKRHGPGPREARGARPGLRVPKTLVLVVAAVLLLVS  -2
 -1  AESALITQQDLAPQQRVAPQQKRSSPSEGLCPPGHHISEDGRDCISCKYG  49
 50  QDYSTEWNDLLFCLRCTRCDSGEVELSPCTTTRNTVCQCEEGTFREEDSP  99
100  EMCRKCRTGCPRGMVKVGDCTPWSDIECVHKESGIIIGVTVAAVVLIVAV  149
150  FVCKSLLWKKVLPYLKGICSGGGGDPERVDRSSQRPGAEDNVLNEIVSIL  199
200  QPTQVPEQEMEVQEPAEPTGVNMLSPGESEHLLEPAEAERSQRRRLLVPA  249
250  NEGDPTETLRQCFDDFADLVPFDSWEPLMRKLGLMDNEIKVAKAEAAGHR  299
300  DTLYTMLIKWVNKTGRDASVHTLLDALETLGERLAKQKIEDHLLSSGKFM  349
350  YLEGNADSAMS*  360
```

B

```
-63  MQGVKERVLPLGNSGDRAPRPPDGRGRVRPRTQDGVGNETMARIPKTLKF  -14
-13  VVVIVAVLLPVLAYSATTARQEEVPQQTVAPQQQRHSFKGEECPAGSHRS  37
 38  EHTGACNPCTEGVDYTNASNNEPSCFPCTVCKSDQKHKSSCTMTRDTVCQ  87
 88  CKEGTFRNENSPEMCRKCSRCPSGEVQVSNCTSWDDIQCVEEFGANATVE  137
138  TPAAEETMNTSPGTPAPAAEETMNTSPGTPAPAAEETMTTSPGTPAPAAE  187
188  ETMTTSPGTPAPAAEETMTTSPGTPASSHYLSCTIVGIIVLIVLLIVFV*  236
```

C

```
DR5      273  SWEPLMRKLGLMDNEIK.VAKAEAAGHRDTLYTMLIKWVNKTG.RDASVH  320
DR4      356  SWDQLMEQL LTKNEII.VVRAGTAGPGDALYAMLMKWVNKTG.RNASIH  403
DR3      346  RWKKEVRTLGLREAEIEAVEVEIGR.FRDQQYEMLKRWRQQQP...AGLG  391
TNFR-1   330  RKKEEYHRLGLSDHEIDRLELQNGRCLREAQYSMLATWRRRTPRREATLE  379
FAS      228  QVEGEMHRNGVNEAKSDSIKNDNVQDTAEQKVQLLRNWHQLHGKKEA.YD  276
CAR1     269  EWKREGHALDLQENDLY.LAEQHDRVSCEPFYQMLNTWLNQQG.SKASVN  313

DR5      321  TLLDAIETLGERLAKQKIE  339
DR4      404  TLLDAIETMGERHAKEKIQ  422
DR3      392  AVYAAEIDMGLDGCVE LR  410
TNFR-1   380  LDGRVLRDMDLLGCLEDIE  398
FAS      277  TLIKSDLKKANDCTLAKKIQ  293
CAR1     314  TLLETLPRIGLSGVADLLA  333
```

FIGS. 1A-C

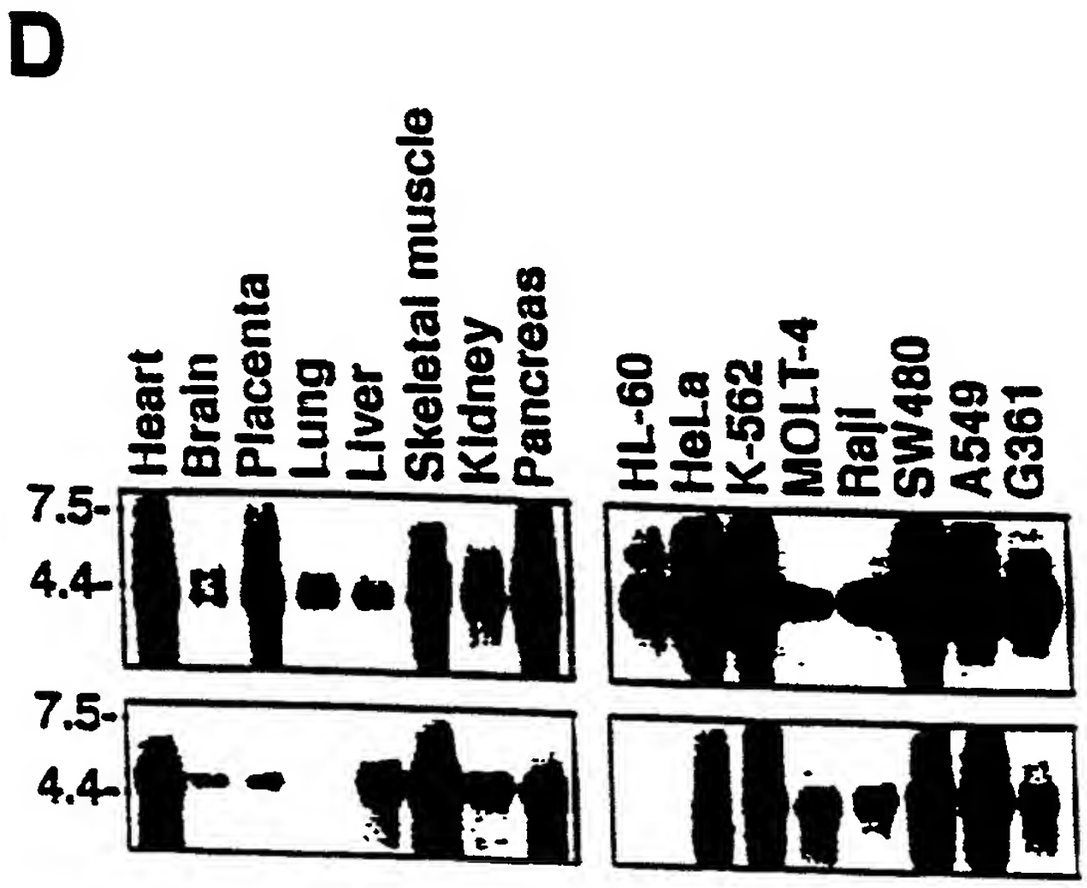

D
Heart
Brain
Placenta
Lung
Liver
Skeletal muscle
Kidney
Pancreas
HL-60
HeLa
K-562
MOLT-4
Raji
SW480
A549
G361
7.5-
4.4-
7.5-
4.4-

FIG. 1D

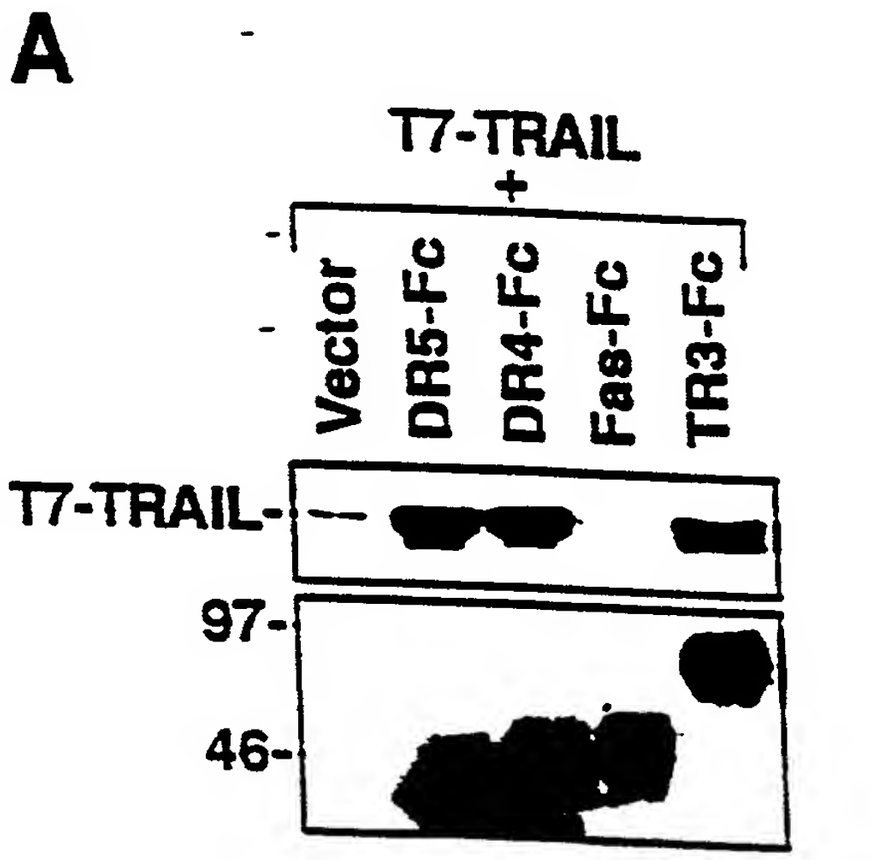


FIG. 2A

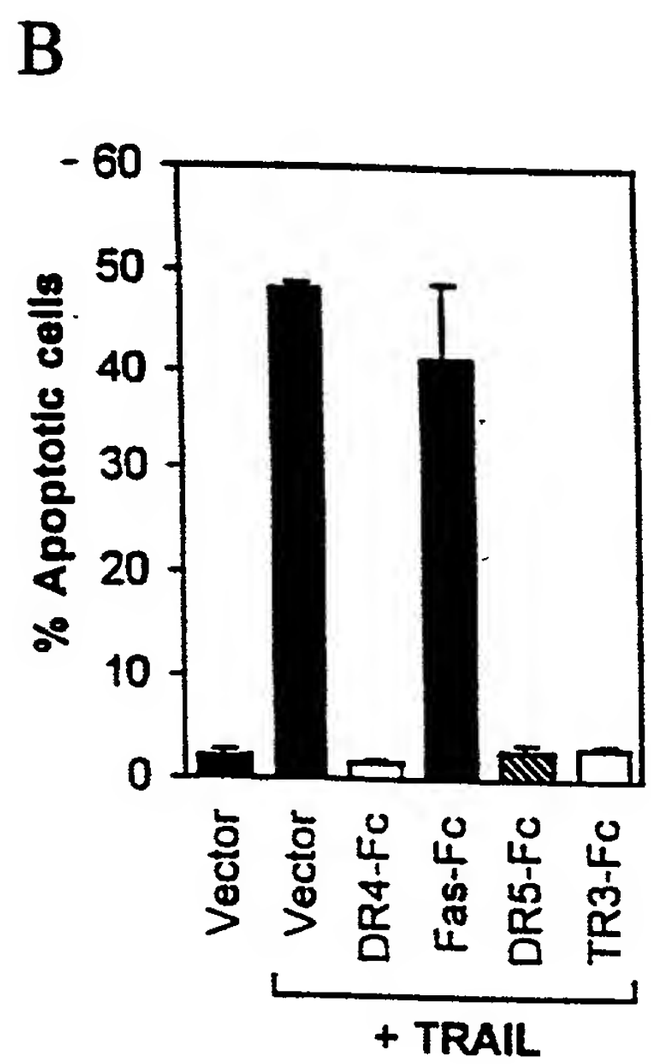
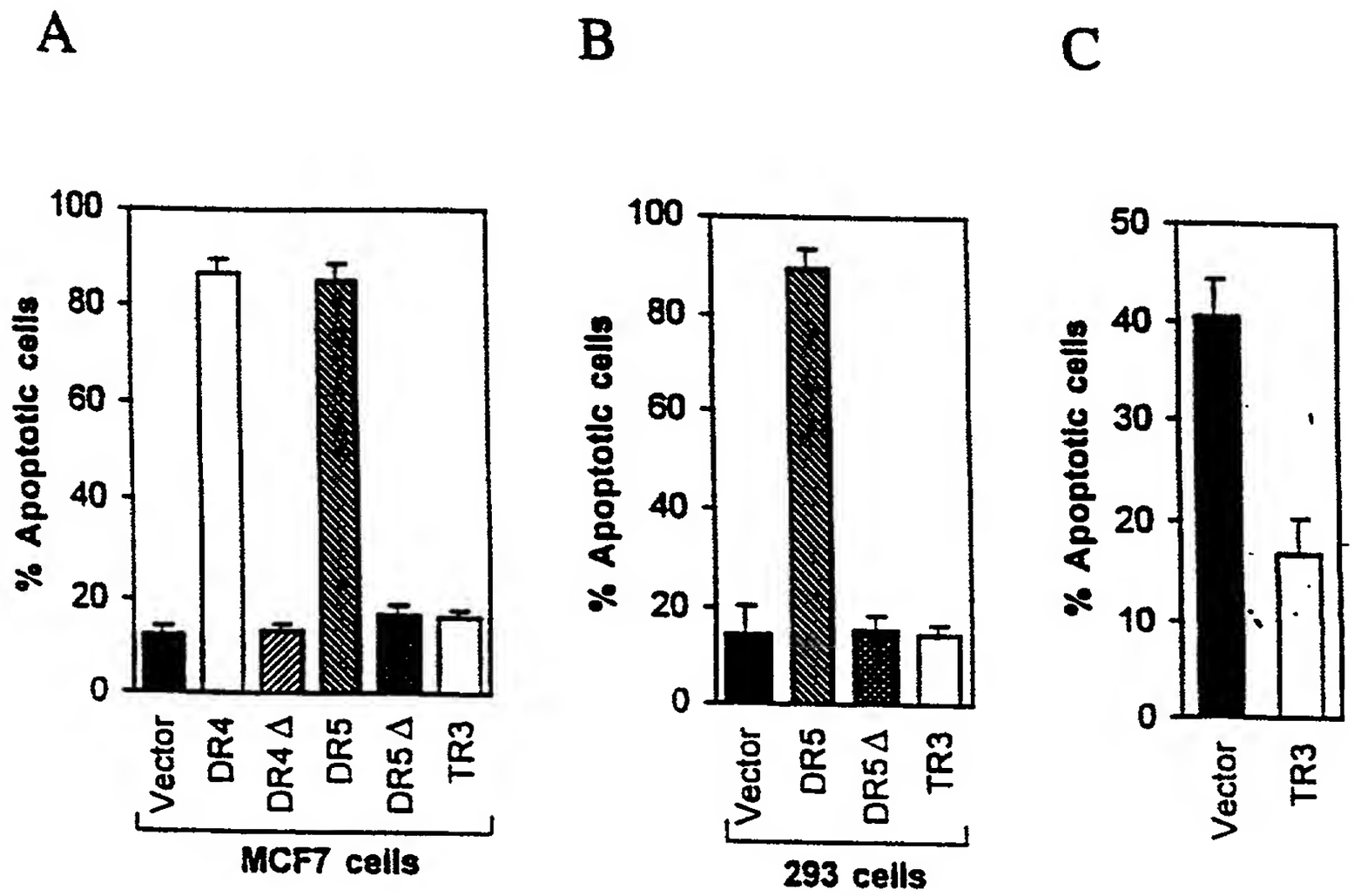
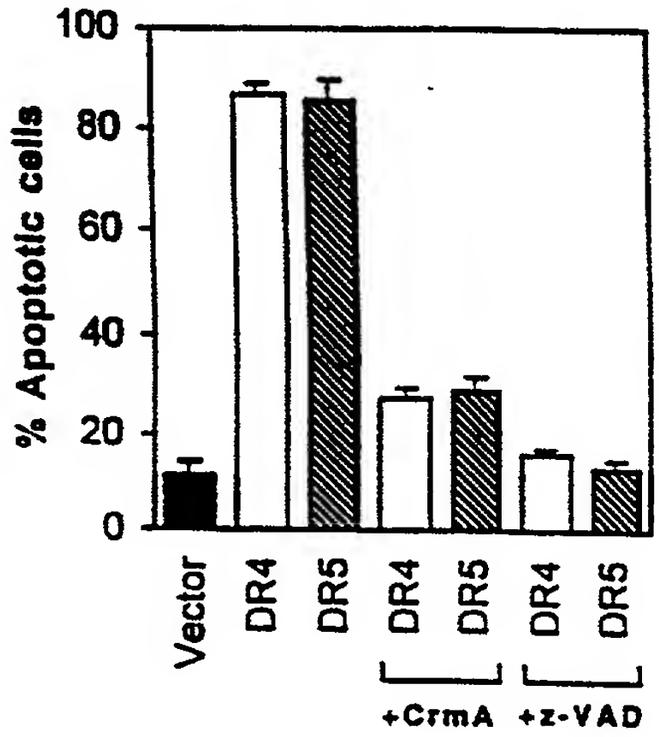

B
% Apoptotic cells
60
50
40
30
20
10
0
Vector
Vector
DR4-Fc
Fas-Fc
DR5-Fc
TR3-Fc
+ TRAIL

FIG. 2B

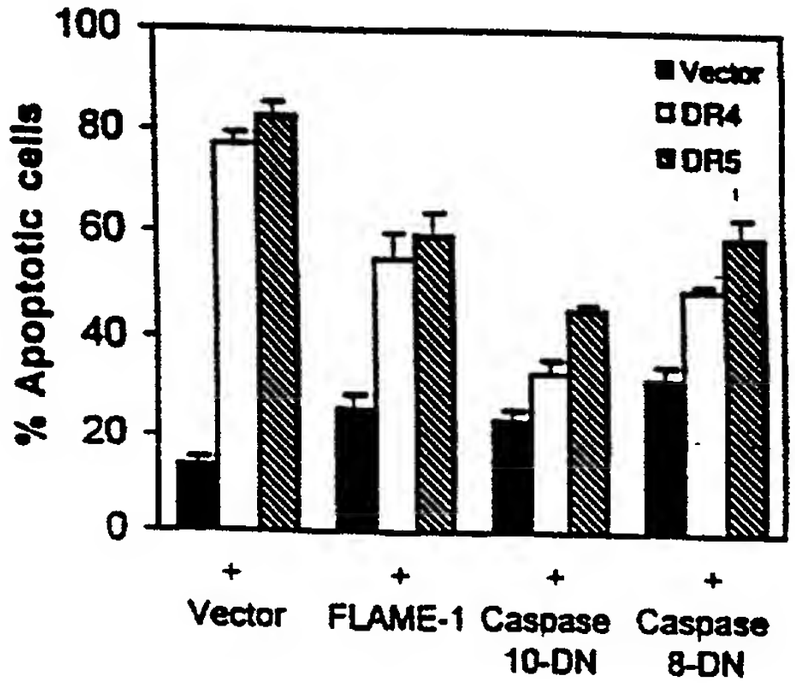

A
B
C
% Apoptotic cells
100
80
60
40
20
0
50
40
30
20
10
Vector
DR4
DR4 Δ
DR5
DR5 Δ
TR3
MCF7 cells
293 cells

FIGS. 3A-C

D


100
80
60
40
20
0
% Apoptotic cells
Vector
DR4
DR5
DR4
DR5
DR4
DR5
+CrmA
+z-VAD

E


100
80
60
40
20
0
% Apoptotic cells
Vector
DR4
DR5
+
+
+
+
Vector
FLAME-1
Caspase 10-DN
Caspase 8-DN

FIGS. 3D-E

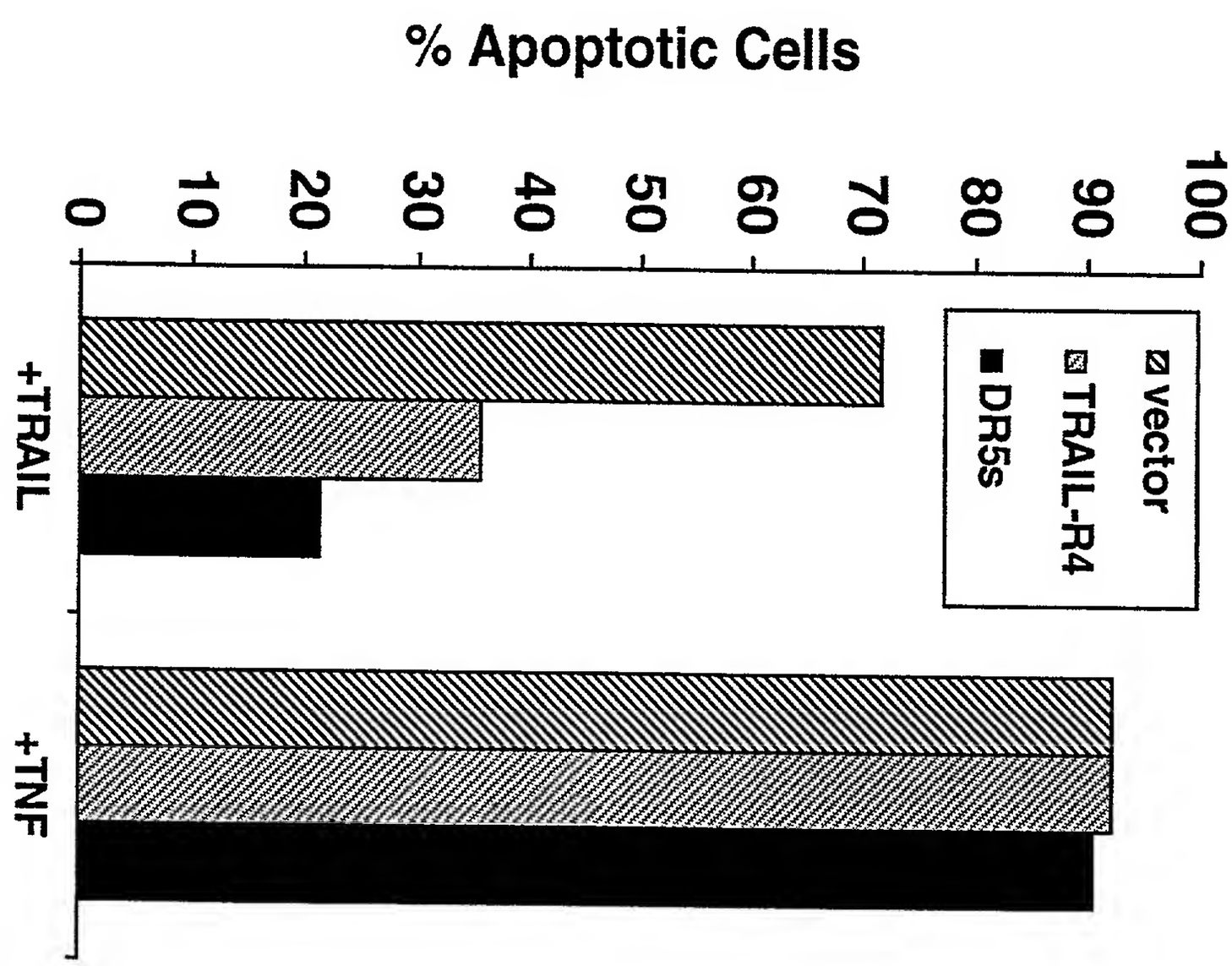
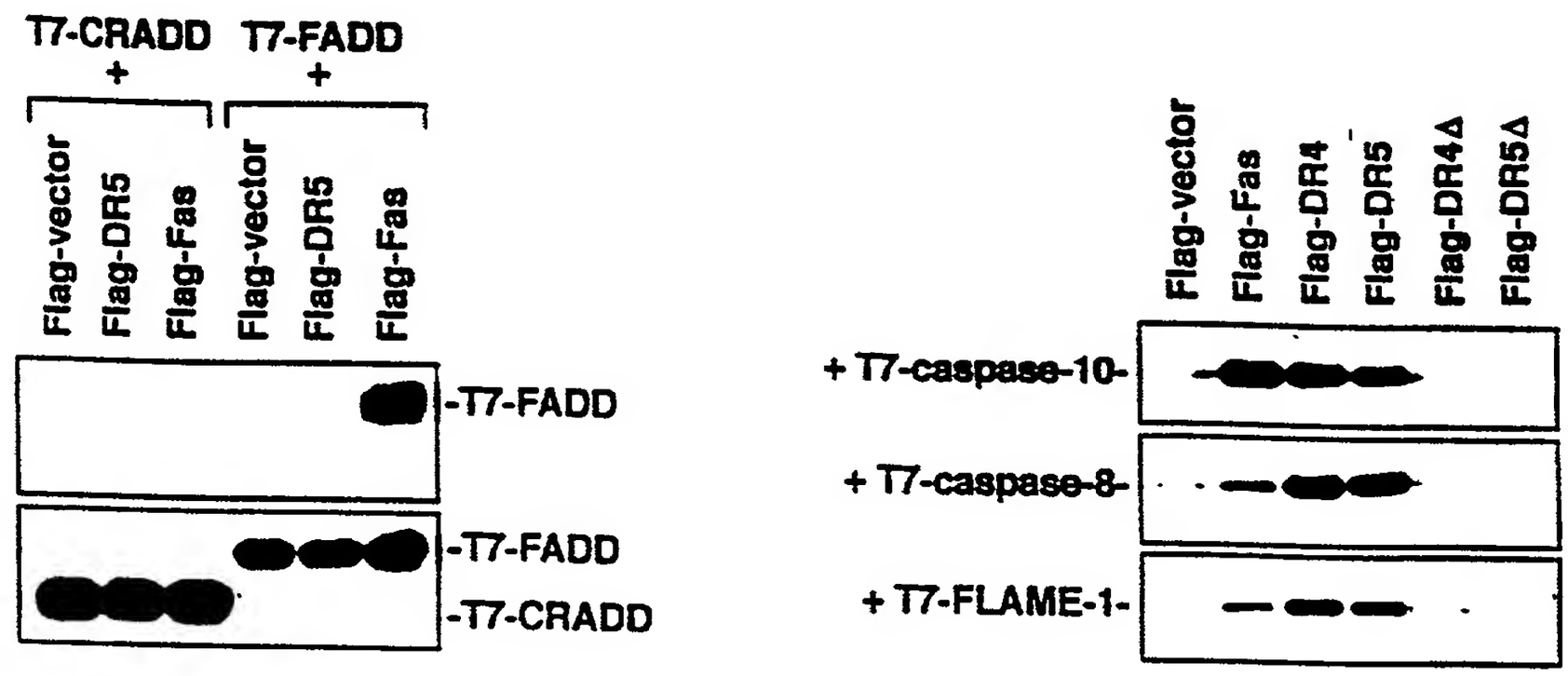

% Apoptotic Cells
0
10
20
30
40
50
60
70
80
90
100
vector
TRAIL-R4
DR5s
+TRAIL
+TNF

FIG. 3F


A
T7-CRADD +
T7-FADD +
Flag-vector
Flag-DR5
Flag-Fas
Flag-vector
Flag-DR5
Flag-Fas
-T7-FADD
-T7-FADD
-T7-CRADD
B
Flag-vector
Flag-Fas
Flag-DR4
Flag-DR5
Flag-DR4Δ
Flag-DR5Δ
+ T7-caspase-10-
+ T7-caspase-8-
+ T7-FLAME-1-

FIGS. 4A-B

```
   1  ATGGAACAACGGGGACAGAACGCCCCGGCCGCTTCGGGGGCCCGGAAAAGGCACGGCCCA   60
   1  M  E  Q  R  G  Q  N  A  P  A  A  S  G  A  R  K  R  H  G  P    20

  61  GGACCCAGGGAGGCGCGGGGAgCCAGGCCTGGGCTCCGGGTCCCCAAGACCCTTGTGCTC  120
  21  G  P  R  E  A  R  G  A  R  P  G  L  R  V  P  K  T  L  V  L    40

 121  GTTGTCGCCGCGGTCCTGCTGTTGGTCTCAGCTGAGTCTGCTCTGATCACCCAACAAGAC  180
  41  V  V  A  A  V  L  L  L  V  S  A  E  S  A  L  I  T  Q  Q  D    60

 181  CTAGCTCCCCAGCAGAGAGTGGCCCCACAACAAAAGAGGTCCAGCCCCTCAGAGGGATTG  240
  61  L  A  P  Q  Q  R  V  A  P  Q  Q  K  R  S  S  P  S  E  G  L    80

 241  TGTCCACCTGGACACCATATCTCAGAAGACGGTAGAGATTGCATCTCCTGCAAATATGGA  300
  81  C  P  P  G  H  H  I  S  E  D  G  R  D  C  I  S  C  K  Y  G    100

 301  CAGGACTATAGCACTCACTGGAATGACCTCCTTTTCTGCTTGCGCTGCACCAGGTGTGAT  360
 101  Q  D  Y  S  T  H  W  N  D  L  L  F  C  L  R  C  T  R  C  D    120

 361  TCAGGTGAAGTGGAGCTAAGTCCCTGCACCACGACCAGAAACACAGTGTGTCAGTGCGAA  420
 121  S  G  E  V  E  L  S  P  C  T  T  T  R  N  T  V  C  Q  C  E    140

 421  GAAGGCACCTTCCGGGAAGAAGATTCTCCTGAGATGTGCCGGAAGTGCCGCACAGGGTGT  480
 141  E  G  T  F  R  E  E  D  S  P  E  M  C  R  K  C  R  T  G  C    160

 481  CCCAGAGGGATGGTCAAGGTCGGTGATTGTACACCCTGGAGTGACATCGAATGTGTCCAC  540
 161  P  R  G  M  V  K  V  G  D  C  T  P  W  S  D  I  E  C  V  H    180

 541  AAAGAATCAGGTACAAAGCACAGTGGGGAAGCCCCAGCTGTGGAGGAGACGGTGACCTCC  600
 181  K  E  S  G  T  K  H  S  G  E  A  P  A  V  E  E  T  V  T  S    200

 601  AGCCCAGGGACTCCTGCCTCTCCCTGTTCTCTCtCAGGCATCATCATAGGAGTCACAGTT  660
 201  S  P  G  T  P  A  S  P  C  S  L  S  G  I  I  I  G  V  T  V    220

 661  GCAGCCGTAGTCTTGATTGTGGCTGTGTTTGTTTGCAAGTCTTTACTGTGGAAGAAAGTC  720
 221  A  A  V  V  L  I  V  A  V  F  V  C  K  S  L  L  W  K  K  V    240

 721  CTTCCTTACCTGAAAGGCATCTGCTCAGGTGGTGGTGGGGACCCTGAGCGTGTGGACAGA  780
 241  L  P  Y  L  K  G  I  C  S  G  G  G  G  D  P  E  R  V  D  R    260

 781  AGCTCACAACGACCTGGGGCTGAGGACAATGTCCTCAATGAGATCGTGAGTATCTTGCAG  840
 261  S  S  Q  R  P  G  A  E  D  N  V  L  N  E  I  V  S  I  L  Q    280

 841  CCCACCCAGGTCCCTGAGCAGGAAATGGAAGTCCAGGAGCCAGCAGAGCCAACAGGTGTC  900
 281  P  T  Q  V  P  E  Q  E  M  E  V  Q  E  P  A  E  P  T  G  V    300

 901  AACAAAACCgGGCgAgATGCCTCTGTCCACACCCTGCTGGATGCCTTGGAgACgCTGGGA  960
 301  N  K  T  G  R  D  A  S  V  H  T  L  L  D  A  L  E  T  L  G    320

 961  gAgAgACTTGCCAAGCAGAAGATTGAGGACCACTTGTTGAGCTCTGGAAAGTTCATGTAT 1020
 321  E  R  L  A  K  Q  K  I  E  D  H  L  L  S  S  G  K  F  M  Y    340

1021  CTAGAAGGTAATGCAGACTCTGCCATGTCCTAA  1053
 341  L  E  G  N  A  D  S  A  M  S  *     351
```

FIG. 5

```
DR5s   1 MEQRGQNAPAASGARKRHGPGPREARGARPGLRVPKTLVLVVAAVLLLVS 50
         ||||||||||||||||||||||||||||||||||||||||||||||||||
DR5    1 MEQRGQNAPAASGARKRHGPGPREARGARPGLRVPKTLVLVVAAVLLLVS 50

      51 AESALITQQDLAPQQRVAPQQKRSSPSEGLCPPGHHISEDGRDCISCKYG 100
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 AESALITQQDLAPQQRVAPQQKRSSPSEGLCPPGHHISEDGRDCISCKYG 100

     101 QDYSTHWNDLLFCLRCTRCDSGEVELSPCTTTRNTVCQCEEGTFREEDSP 150
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 QDYSTHWNDLLFCLRCTRCDSGEVELSPCTTTRNTVCQCEEGTFREEDSP 150

     151 EMCRKCRTGCPRGMVKVGDCTPWSDIECVHKESGTKHSGEAPAVEETVTS 200
         |||||||||||||||||||||||||||||||
     151 EMCRKCRTGCPRGMVKVGDCTPWSDIECVHKE..................  182

     201 SPGTPASPCSLSGIIIGVTVAAVVLIVAVFVCKSLLWKKVLPYLKGICSG 250
                 ||||||||||||||||||||||||||||||||||||||||||||
     183 ..........SGIIIGVTVAAVVLIVAVFVCKSLLWKKVLPYLKGICSG 221

     251 GGGDPERVDRSSQRPGAEDNVLNEIVSILQPTQVPEQEMEVQEPAEPTG. 299
         |||||||||||||||||||||||||||||||||||||||||||||||||
     222 GGGDPERVDRSSQRPGAEDNVLNEIVSILQPTQVPEQEMEVQEPAEPTGV 271

                                      .
                                      .
                                      .

     300 .....................................VNKTGRDASVH 310
                                              ||||||||||||
     322 FDSWEPLMRKLGLMDNEIKVAKAEAAGHRDTLYTMLIKWVNKTGRDASVH 371

     311 TLLDALETLGERLAKQKIEDHLLSSGKFMYLEGNADSAMS 350
         |||||||||||||||||||||||||||||||||||||||
     372 TLLDALETLGERLAKQKIEDHLLSSGKFMYLEGNADSAMS 411
```

FIG. 6